

What is claimed is:

1. An isolated nucleic acid molecule encoding an OLD-35 or OLD-64 protein.
- 5 2. The isolated nucleic acid molecule of claim 1 wherein the nucleic acid comprises a nucleic acid having a sequence substantially the same as set forth in SEQ. ID. No.39 or 19.
- 10 3. An isolated nucleic acid molecule encoding an OLD-137, OLD-139, OLD-142, or OLD-175 protein.
4. The isolated nucleic acid molecule of claim 3 wherein the nucleic acid comprises a nucleic acid having a sequence substantially the same as set forth in SEQ. ID. Nos.31, 32, 34 or 38.
- 15 5. An isolated nucleic acid molecule of claim 1, or 3, wherein the nucleic acid is DNA, genomic DNA, cDNA, synthetic DNA, or RNA.
- 20 6. A nucleic acid molecule comprising a nucleic acid molecule of at least 15 nucleotides capable of specifically hybridizing with a sequence included within the sequence of the nucleic acid molecule of claim 1, or 3.
- 25 7. A nucleic acid molecule of claim 6 wherein the nucleic acid is DNA, genomic DNA, cDNA, synthetic DNA or RNA.
- 30 8. An antisense nucleic acid molecule comprising a sequence complementary to the nucleic acid of claim 1 or 3.
- 35 9. The antisense nucleic acid molecule of claim 8, capable of inhibiting the expression of the hybridized

gene.

10. An isolated nucleic acid molecule of claim 1, 3, or 8 operatively linked to a promoter of RNA transcription.

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11. A vector which comprises the isolated nucleic acid molecule of claim 1, 3 or 8.

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12. A host vector system for the production of a protein having the biological activity of OLD-35 or OLD-64 protein which comprises the vector of claim 11 in a suitable host.

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13. A host vector system for the production of a protein having the biological activity of OLD-137, OLD-139, OLD-142, OLD-175 protein which comprises the vector of claim 11 in a suitable host.

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14. A method of producing a protein having the biological activity of OLD-35, OLD-64 OLD-137, OLD-139, OLD-142, OLD-175 protein which comprises growing the host vector system of claim 12, or 13 under conditions permitting production of the protein and recovering the protein so produced.

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15. A purified, OLD-35 protein.

16. A purified, OLD-64 protein.

30 17. A purified, OLD-137 protein.

18. A purified, OLD-139 protein.

19. A purified, OLD-142 protein.

20. A purified, OLD-175 protein.

Subs 5
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21. A protein encoded by the isolated nucleic acid molecule of claim 1 or 3.

22. An antibody or antigen-binding fragment thereof that specifically binds to OLD-35, OLD-64, OLD-137, OLD-139, OLD-142 or OLD-175 protein.

10 23. A monoclonal antibody of claim 22.

24. A method of inhibiting growth of cancer cells comprising contacting the cancer cells with an amount of purified OLD-35, or OLD-64 protein or a portion thereof effective to inhibit growth of cancer cells.

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25. A method for reversing the cancerous phenotype of a cancer cell which comprises introducing a nucleic acid comprising an Old-35 or Old-64 gene or a portion thereof into the cell under conditions permitting the expression of the gene so as to thereby reverse the cancerous phenotype of the cell.

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26. A method for reversing the cancerous phenotype of a cancer cell in a subject which comprises introducing a nucleic acid molecule comprising an Old-35 or Old-64 gene or a portion thereof into the subject's cancerous cell under conditions permitting expression of the gene in the subject's cell so as to thereby reverse the cancerous phenotype of the cell.

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27. The method according to claim 25 or 26, wherein the nucleic acid molecule comprises a vector.

35 28. The method according to claim 25 or 26, wherein the Old-35 or Old-64 gene is linked to a regulatory

element such that its expression is under the control of the regulatory element.

29. The method according to claim 26, wherein the regulatory element is a tissue specific regulatory element.

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30. The method of claim 25 or 26, wherein the nucleic acid molecule is introduced into the cells by naked DNA technology, adenovirus vector, adeno-associated virus vector, Epstein-Barr virus vector, Herpes virus vector, attenuated HIV vector, retroviral vectors, vaccinia virus vector, liposomes, antibody-coated liposomes, mechanical or electrical means.

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31. A method for reversing the cancerous phenotype of a cancer cell which comprises introducing OLD-35 or OLD-64 protein into the cancerous cell so as to thereby reverse the cancerous phenotype of the cell.

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32. A method for reversing the cancerous phenotype of a cancer cell in a subject which comprises introducing OLD-35 or OLD-64 protein into the subject's cancerous cell so as to thereby reverse the cancerous phenotype of the cell.

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33. The method according to claim 25, 26, 31 or 32, wherein the cancer cell is a breast, cervical, colon, pancreatic, thyroid, skin, brain, prostate, nasopharyngeal, lung, glioblastoma multiforme, lymphoma, leukemia, connective tissue, nervous system cell or basal cell.

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34. A pharmaceutical composition which comprises an amount of a nucleic acid molecule comprising Old-35, Old-64 gene or portion thereof effective to reverse the cancerous phenotype of a cancer cell and a

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pharmaceutically acceptable carrier.

35. The pharmaceutical composition of claim 34, wherein
the nucleic acid molecule comprises a vector.

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36. The pharmaceutical composition of claim 35, wherein
the vector is an adenovirus vector, adeno-associated
virus vector, Epstein-Barr virus vector, Herpes virus
vector, attenuated HIV vector, retrovirus vector or
10 vaccinia virus vector.

37. A pharmaceutical composition comprising an amount of
OLD-35 or OLD-64 protein effective to reverse the
cancerous phenotype of a cancer cell and a
15 pharmaceutically acceptable carrier.

38. The pharmaceutical composition of claim 34 or 36,
wherein the cancer cell is a breast, cervical, colon,
pancreatic, thyroid, skin, brain, prostate,
20 nasopharyngeal, lung, glioblastoma multiforme,
lymphoma, leukemia, connective tissue, nervous system
or basal cell.

39. A method of determining whether a cell is senescent
25 comprising measurement of the expression of the Old-35
gene, wherein the expression of the Old-35 gene
indicates that the cell is senescent.

40. The method of claim 39, wherein the expression of the
30 Old-35 gene is measured by the expression of Old-35
specific RNA.

41. The method of claim 39, wherein the expression of the
35 Old-35 gene is measured by the expression of the OLD-
35 protein.

42. A method of determining whether a cell is terminally differentiated comprising measurement of the expression of the Old-35 gene, wherein the expression of the Old-35 gene indicates that the cell is terminally differentiated.

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43. The method of claim 42, wherein the expression of the Old- 35 gene is measured by the expression of Old-35 specific RNA.

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44. The method of claim 42, wherein the expression of the Old-35 gene is measured by the expression of OLD-35 protein.

15 45. A method of determining whether a cell is growth arrested comprising measurement of the expression of the Old-35 gene, wherein the expression of the Old-35 gene indicates that the cell is growth arrested.

20 46. The method of claim 45, wherein the expression of the Old-35 gene is measured by the expression of old 35 specific RNA.

25 47. The method of claim 45, wherein the expression of the Old-35 gene is measured by the expression of OLD-35 protein.

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48. A method of inhibiting growth of cancer cells comprising contacting the cancer cells with an amount of purified OLD-64 protein effective to inhibit growth of cancer cells.

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49. A method of inhibiting growth of cancer cells comprising contacting the cancer cells with an amount of purified OLD-64 protein effective to inhibit growth of cancer cells.

50. A method of determining whether a cell is senescent comprising measurement of the expression of the Old-64 gene, wherein the expression of the Old-64 gene indicates that the cell is senescent.

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51. The method of claim 50, wherein the expression of the old-64 gene is measured by the expression of Old-64 specific RNA.

10 52. The method of claim 50, wherein the expression of the Old-64 gene is measured by the expression of the OLD-64 protein.

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53. A method of determining whether a cell is terminally differentiated comprising measurement of the expression of the Old-64 gene, wherein the expression of the Old-64 gene indicates that the cell is terminally differentiated.

20 54. The method of claim 53, wherein the expression of the Old-64 gene is measured by the expression of Old-64 specific RNA.

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55. The method of claim 53, wherein the expression of the Old-64 gene is measured by the expression of the OLD-64 protein.

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56. A method of determining whether a cell is growth arrested comprising measurement of the expression of the Old-64 gene, wherein the expression of the Old-64 gene indicates that the cell is growth arrested.

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57. The method of claim 56, wherein the expression of the Old- 64 gene is measured by the expression of Old-64 specific RNA.

58. The method of claim 56, wherein the expression of the Old-64 gene is measured by the expression of the OLD-64 protein.

5 59. A method of regenerating tissues comprising contacting the tissue with an inhibitor of OLD-35 or OLD-64 protein or a portion thereof at a concentration effective to regenerate said tissues.

10 60. A method of anti-aging in a cell comprising contacting the cell with an agent for inhibiting expression of Old-35 or Old-64 gene at a concentration effective to reverse the aging process in the cell.

15 61. A pharmaceutical composition for stimulating cell growth comprising a pharmaceutically acceptable carrier and purified Old-35 or Old-64 suppressant at a concentration effective to stimulate cell growth.

20 62. A method for screening the presence of interferon alpha or beta of a sample comprising steps of:
(a) contacting the sample with cells under conditions permitting expression of Old-35 or Old-64 gene in the presence of interferon alpha or beta; and
25 (b) determining the expression of the Old-35 or the Old-64 gene, an increase of expression indicates the presence of interferon alpha or beta.

30 63. A method for detection of the secretion of interferon alpha or beta comprising steps of:
(a) obtaining an appropriate sample from the subject; and
35 (b) detecting expression of Old-35 or Old-64 gene, the expression of the Old-35 or the

Old-64 gene indicating the secretion of interferon in a subject.

64. A method for monitoring chemotherapy of a subject comprising steps of:

5 (a) obtaining an appropriate sample from the subject; and
(b) detecting expression of Old-35 or Old-64 gene, the expression of Old-35 or Old-64
10 gene indicating that the chemotherapy is effective.

65. A method for diagnosis of the proliferating stage of a tumor from a subject comprising steps of:

15 (a) obtaining an appropriate sample from the subject; and
(b) detecting expression of the Old-35 or the Old-64 gene, the expression of the Old-35 or the Old-64 gene indicating that the tumor is
20 not at a proliferating stage.

66. A kit for diagnosis of the proliferating stage of a tumor, comprising a nucleic acid molecule capable of specifically hybridizing to the nucleic acid molecule of the Old-35 or the Old-64 gene.

67. A kit for diagnosis of the proliferating stage of a tumor, comprising antibody capable of specifically recognizing OLD-35 or OLD-64 protein.

30 68. A method for identifying an agent that modulates the expression of the Old-35 or the Old-64 gene, comprising:

35 (a) contacting a candidate agent with a cell transformed or transfected with a reporter gene under the control of a Old-35 or Old-64

5 promoter or a regulatory element thereof under conditions and for a time sufficient to allow the candidate agent to directly or indirectly alter expression of the promoter or regulatory element thereof; and

10 (b) determining the effect of the candidate agent on the level of reporter protein produced by the cell, thereby identifying an agent that modulates expression of Old-35 or 64 gene.

15 69. A method of identifying compounds that induce proliferation or cancerous phenotype, comprising: exposing cell comprising the promoter of Old-35 or Old-64 to the compound and identifying compounds that suppress the Old-35 or 64 promoter.

20 70. A method of identifying compounds that induces senescence, or terminal differentiation, comprising: exposing the cell comprising the promoter of Old-35 or Old-64 to the compound and identifying compounds that activate the Old-35 or 64 promoter.

25 71. A method of identifying genes which are common to the pathway of senescence and terminal differentiation comprising steps of:

30 (a) obtaining a subtracted library which is enriched for genes expressed in terminal differentiation;

35 (b) screening the library with senescent probe to identify novel genes which are expressed during senescence and terminal differentiation; and

(c) examining the biological activity of the identified gene to determine whether it is expressed during senescence and terminal differentiation.

72. A method of identifying genes which are common to the pathway of senescence and terminal differentiation comprising steps of:

5 (a) obtaining a subtracted library which is enriched for genes expressed in senescence;

(b) screening the library with terminal differentiation probe to identify novel genes which are expressed during senescence and terminal differentiation; and

10 (c) examining the biological activity of the identified gene to determine whether it is expressed during senescence and terminal differentiation.

15 73. The gene identified by the method of claim 71 or 72.

74. A method of degrading specific RNAs in a cell comprising induction of the expression of Old-35 gene.

20 74. A method of degrading specific RNAs in a cell comprising introducing a vector into the cell comprising the Old-35 gene.

75. Expression of Old-35 can be used as diagnostic indicator of cellular senescence, terminal differentiation and/or growth suppression.

25 (a) can be used to determine if a cell has lost proliferative ability and become senescent.

30 76. Expression of Old-35 can be used as a marker to identify drugs or small molecules that will induce senescence, e.g., to inhibit cancer cell growth or abnormal proliferative states (such as psoriasis, hemangioblastoma, etc.)

35 77. Expression of Old-35 can be used to identify drugs or

small molecules that will inhibit senescence, possible uses including stimulating tissue regrowth, repair and regeneration.

5 78. Expression of Old-35 can be used as a marker to identify drugs or small molecules that will induce terminal cell differentiation, e.g., to inhibit cancer cell growth or abnormal proliferative states (such as psoriasis, hemangioblastoma, etc.).

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79. Expression of Old-35 can be used to identify drugs or small molecules that will inhibit terminal differentiation, possible uses including stimulating tissue regrowth, repair and regeneration.

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80. Expression of Old-35 can be used as marker for detecting cytokines, specifically type I interferons, in biological samples. Since type I interferon, including leukocyte and fibroblast interferons, which activate gene expression through the well characterized Jak and Stat kinase pathways, this gene can be used to monitor for drugs and small molecules that activate these important pathways.

25 81. The combination of Old-35 with other interacting proteins can be used to target the differentiation of specific target cells. This can result in the reprogramming of pluripotent stem cells to terminally differentiated end cells.

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82. Old-35 can be used to selectively stabilize specific mRNAs possibly containing AU rich 3' UTRs (untranslated regions). This effect can result in the sustained expression of genes potentiating or inhibiting cell growth. It could also result in the stabilizing of cytokine genes resulting in increased biological and immunological activity.

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83. Old-35 can be used as part of a methodology to polymerize random NTPs into nucleic acids.

5 84. Old-35 can be used to induce the degradation of specific mRNAs.